

Synthesis of 4-*tert*-octylphenol and 4-cumylphenol by metal triflate and metal triflimidate catalysts

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Metal triflates and metal triflimidates are shown to catalyse efficiently the Friedel–Crafts alkylation of phenol with alkenes. Bismuth, copper and scandium triflates lead to very good yields with excellent *para*-selectivities.

Keywords. catalysis, metal triflate, bismuth, Friedel–Crafts alkylation

The alkylation of phenols is an industrial process of great importance, notably for the production of lubricants and antioxidants.¹ Alkylphenols can be used directly or as intermediates, and molecules like 4-*t*-octylphenol and 4-cumylphenol are of industrial interest as final products. Historically, alkylphenols are manufactured by the reaction between the low cost raw materials phenols and alkenes, in the presence of an acid catalyst (*i.e.* trifluoromethanesulfonic acid, oleum, boron trifluoride, sulfonic resins, *p*-toluenesulfonic acid, methanesulfonic acid).

This Friedel–Crafts alkylation is also of interest for the synthesis of fine chemicals, particularly if good regioselectivity such as selective *para*-orientation can be achieved.

Metal triflates, and notably rare earth metal triflates, are now common tools for organic synthesis. Their Lewis acid properties lead to the catalysis of a large number of reactions.² Amongst them, it has recently been demonstrated that bismuth triflate presents great potential.³ In particular, several Friedel–Crafts reactions have been explored. Le Roux and coworkers have opened the way for this kind of bismuth triflate catalysed reactions reporting remarkable results for the aryl- and alkyl-sulfonylation of arenes.^{4,5} Other Friedel–Crafts alkylations have been realised with some metal triflates^{2,6,7} including that of bismuth^{8,9} with moderate to good yields. To our knowledge, one example of Friedel–Crafts alkylation of phenol with alkenes using scandium triflate has been reported so far, leading to a good yield and a moderate selectivity, with necessity of employing an expensive solvent, a long reaction time and a large amount of catalyst (10 mol%).¹⁰

We present here the solventless alkylation of phenol using some homoleptic metal triflates and metal triflimidates to obtain two products of industrial interest.

The catalysts were synthesised according to literature procedures from metal oxides and triflic or bis-(trifluoromethane)-sulfonimide acids.^{2,11,12} Note that the synthesis is straightforward but the drying of some products in order to obtain free-flowing powders is sometimes difficult, in particular for triflimidate derivatives.

Screening of several catalysts was first carried out to check whether this reaction is feasible with such compounds.

The chosen reaction for this screening was the alkylation of phenol by 2,4,4-trimethylpent-1-ene to synthesise 4-*tert*-octylphenol (Scheme 1).

The amount of catalyst was 1 mol% of metal complex with respect to the alkene, taking into consideration the water content for each derivative (measured by Karl–Fisher titration, always below three water molecules per metal atom). To limit the formation of dialkylated products, the phenol: alkene ratio was set to 2:1. The general procedure can be described as follows. A mixture of phenol (45 mmol) and catalyst (0.22 mmol) was warmed at 60°C under inert gas. The alkene (22.5 mmol) was added and the mixture was maintained at 60°C under stirring. Yields were determined by GC using internal standards. Dialkylated yields were always below 2%. The results are presented in Fig. 1.

A blank experiment showed that, under these conditions, no product is obtained without catalyst. It appeared that the four triflimidate derivatives lead to the production of alkylated phenol, with very good *para/ortho* ratios ranging from 12 to 20. Nevertheless, significant amounts of alkene dimers were found at the end of the reaction, and the best yield was only 52% with La(NTf₂)₃.

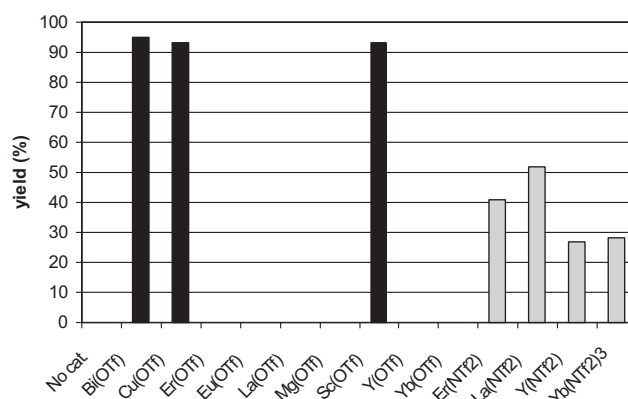
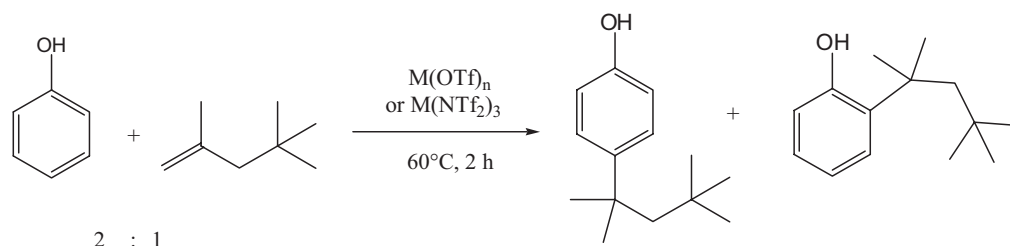


Fig. 1 Screening of catalysts for phenol alkylation with 2,4,4-trimethylpent-1-ene.



Scheme 1 Phenol alkylation with 2,4,4-trimethylpent-1-ene.

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Table 1 Phenol alkylation with Bi(OTf)₃, Cu(OTf)₂ and Sc(OTf)₃

Entry	Alkene	Catalyst	Cat. amount ^a /mol%	Reaction time/min	Yield ^b /%	<i>Para/ortho</i> ^b
1	2,2,4-trimethylpentene	—	—	120	0	—
2	2,2,4-trimethylpentene	Bi(OTf) ₃	1	120	95	> 100
3	2,2,4-trimethylpentene	Cu(OTf) ₂	1	120	93 ^c	52
4	2,2,4-trimethylpentene	Sc(OTf) ₃	1	120	93	37
5	2,2,4-trimethylpentene	Bi(OTf) ₃	1	5	75	17
6	2,2,4-trimethylpentene	Bi(OTf) ₃	1	15	80	20
7	2,2,4-trimethylpentene	Cu(OTf) ₂	1	15	70	10
8	2,2,4-trimethylpentene	Sc(OTf) ₃	1	15	77	16
9	2,2,4-trimethylpentene	Bi(OTf) ₃	0.1	120	77	12
10	2,2,4-trimethylpentene	TA ^d	0.1	120	95	> 100
11	α -methylstyrene	Bi(OTf) ₃	1	5	78	9
12	α -methylstyrene	Cu(OTf) ₂	1	5	77	9
13	α -methylstyrene	Sc(OTf) ₃	1	5	78	6
14	α -methylstyrene	TA	0.1	5	82	9

^aAmount without water content, 1 mol% relative to alkene.^bDetermined by GC using internal standard (chlorobenzene), peak determination was done using pure compounds. 4-*t*-octylphenol (97%) was obtained from Aldrich. 2,4,4-trimethylpent-1-ene (99%), α -methylstyrene, 4-cumylphenol (99%) and phenol (99%) were obtained from Acros.

GC conditions: Varian 3800, 30 m HP-5 column, split (25: 1), FID detector.

^c92% isolated yield (silica gel chromatography). The product was identified by MS and ¹³C and ¹H NMR.^dTA: trifluoromethanesulfonic acid

Alkylation with metal triflates revealed that three out of nine catalysts were also efficient for this reaction. Whereas erbium, europium, lanthanum, magnesium, ytterbium and yttrium complexes did not generate any trace of product, the scandium, copper and bismuth triflates were found to be excellent catalysts. Yields were 95% for bismuth (Table 1, entry 2), and 93% for copper and scandium triflates (Table 1, entries 3 and 4). Moreover, outstanding *para*-selectivities were obtained: *para/ortho* ratios were 37: 1 for Sc(OTf)₃, 52: 1 for Cu(OTf)₂ and greater than 100: 1 for Bi(OTf)₃. Encouraged by these unexpected results, we continued studying this reaction with focus on these three catalysts (Table 1).

After 15 min of reaction, yields were already above 70% for the three catalysts (Table 1, entries 6–8), and using Bi(OTf)₃, a 75% yield was reached after only 5 min (Table 1, entry 5).

Alkylation of α -methylstyrene was also successful using these Bi, Cu and Sc triflate catalysts. After 5 min at 60°C, the yields were respectively 78%, 77% and 78% for the three catalysts (Table 1, entries 11–13). A notable point was the difference observed in regioselectivities. Whereas bismuth and copper triflates lead to a *para/ortho* ratio of 9: 1 like triflic acid (Table 1, entry 14), with scandium triflate it was only 6: 1. After 2 h under these conditions the same yields were obtained but the final regioselectivity dropped to 1.3: 1 for Bi(OTf)₃, and 3.5: 1 for Sc(OTf)₃ while it remained constant for Cu(OTf)₂.

It should be noted that for phenol alkylation with 2,4,4-trimethylpent-1-ene the opposite trend was observed since regioselectivities rose with the time of the experiment in favour of the *para* isomer (e.g. Table 1, entries 2, 5 and 6). These results clearly indicate that the alkylation reaction is reversible.

The possibility that traces of triflic acid have contribution to the observed catalytic effect cannot be ruled out. These traces could come from the synthesis of the metal catalyst or be generated during the reaction for example. Despite our attempts to elucidate the mechanism, it remains unclear at this point.

In conclusion, we have shown that synthesis of 4-*t*-octylphenol and 4-cumylphenol is possible by solvent-free metal triflate and metal triflimidate catalysed alkylation of phenol. Using bismuth, copper and scandium triflates, excellent yields and remarkable *para*-selectivities were achieved.

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